I. *Rejections Under 35 U.S.C. §§ 102 and 103*

The Office rejects claims 1-7 and 9-12 under 35 U.S.C. § 102(b) as anticipated by Furuta *et al.* (Office Action at pages 2-3.) The Office further rejects claims 5-8 and 13-20 under 35 U.S.C. § 103(a) as obvious over Furuta *et al.* (Office Action at pages 3-5.) More specifically, the Office asserts that Furuta *et al.* discloses a therapeutic pharmaceutical composition comprising an effective amount of CPT-11 in combination with an effective amount of a topoisomerase II inhibitor for the treatment of tumors. The Office further asserts that it would be obvious to substitute the presently claimed antibiotics and epipdophyllotoxins for those disclosed by Furuta *et al.* and to treat solid tumors with the composition of Furuta *et al.* Applicant respectfully traverses these rejections and submits that Furuta *et al.* neither anticipates nor renders obvious the presently claimed invention.

By this Amendment, independent claims 1, 2, 11, and 13 are amended to more clearly indicate that the effect of the composition recited in the claims is a synergistic effect in the treatment of solid tumors.

It is well established that, in order for the Office to set forth a *prima facie* case of anticipation of a claim by a reference, that reference must disclose, either literally or inherently, each and every element of the rejected claim. Furthermore, it is well established that, in order for the Office to set forth a *prima facie* case of obviousness over a reference, various factual and legal requirements must be met. Among those requirements is the requirement that the reference upon which the Office relies to assert that the claimed invention would have been obvious must teach each and every element recited in the rejected claim. *In re Royka*, 490 F.2d 981, 180 USPQ 580

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(CCPA 1974). Another requirement is that a person of ordinary skill in the art must have had a reasonable expectation of success in achieving the claimed invention if the prior art were to have been modified as suggested by the Office. *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The reasonable expectation of success must be found in the prior art, and cannot be gleaned from the disclosure of Applicant. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). See MPEP § 2142.

A. Rejection Under 35 U.S.C. § 102

Applicant respectfully submits that Furuta *et al.* does not disclose each and every element of the present claims. Accordingly, Furuta *et al.* does not anticipate the present claims. Furthermore, Furuta *et al.* does not suggest the elements of the present claims that it fails to specifically disclose. Likewise, Furuta *et al.* does not provide a reasonable expectation of successfully treating a solid tumor with a synergistic combination of camptothecin, or a camptothecin derivative, and a topoisomerase II inhibitor, as recited in the present claims.

Although Furuta *et al.* states that treatment with CPT-11 and adriamycin (*i.e.*, doxorubicin) provides synergistic effects, this reference does not, in fact, disclose or suggest a synergistic combination according to the present invention. The present application, at page 5, second full paragraph, defines a synergistic combination of two constituents as one that provides a therapeutic effect that is superior to one or the other constituent of the combination when used at its optimum dose (*i.e.*, highest non-toxic dose). Thus, according to the present invention, the maximum tolerated dose of each individual constituent is determined, and a combination having a superior therapeutic effect is developed based on the maximums identified for each individually.

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Nowhere does Furuta *et al.* disclose or suggest determining the highest non-toxic dose of either CPT-11 or adriamycin/doxorubicin. Likewise, Furuta *et al.* does not disclose or suggest developing a composition comprising the two that has a superior therapeutic effect than either alone (at its highest non-toxic dose). Rather, Furuta *et al.* merely discloses the use of 12.5 mg/kg of CPT-11 in combination with 6.25 mg/kg of adriamycin, administered up to three times each in a dosing regimen (see Table 3). Because Furuta *et al.* fails to determine the highest non-toxic dose of CPT-11 and adriamycin, one cannot conclude that the results reported by Furuta *et al.* demonstrate a synergistic effect. In other words, Furuta *et al.* fails to enable one to intentionally formulate a synergistic composition according to the present claims.

For at least this reason, Furuta *et al.* fails to disclose each and every element of the present claims. Thus, a *prima facie* case of anticipation has not been set forth by the Office. Therefore, Applicant respectfully request that the Office reconsider and withdraw the rejection of claims 1-7 and 9-12 under 35 U.S.C. § 102(b) as anticipated by Furuta *et al.*

B. Rejection Under 35 U.S.C. § 103

Because Furuta *et al.* does not suggest determining the highest non-toxic dose of either CPT-11 or adriamycin alone, or finding a combination that provides a therapeutic effect that is superior to either of these doses, Furuta *et al.* does not suggest a synergistic composition according to the present claims. For at least this reason, Furuta *et al.* fails to render the presently claimed invention obvious.

Furthermore, in rejecting the claims under 35 U.S.C. § 103(a), the Office fails to indicate where or how Furuta *et al.* provides a reasonable expectation of success in achieving a synergistic composition that is useful in treating solid tumors. Furuta *et al.*

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discloses treatment of leukemias. However, this reference does not disclose or suggest treating solid tumors with CPT-11 and adriamycin. The Office minimizes this omission, asserting that one would apply the teachings of Furuta *et al.* to any type of tumor. Applicant respectfully disagrees.

It is widely recognized in the art of tumor therapy that a treatment regimen that is successful against one type of tumor (*e.g.*, leukemias) will not necessarily be successful against other types of tumors (*e.g.*, solid tumors). Thus, even assuming for the sake of argument that one were to be motivated by Furuta *et al.* to apply the teachings of Furuta *et al.* to other cancers, such as solid tumors, that person would have no reasonable expectation of success in treating the solid tumors. Rather, at most, one would see Furuta *et al.* as a mere invitation to attempt to treat solid tumors, not a guarantee of success. In other words, any motivation that Furuta *et al.* might provide would be a motivation to try, not a motivation to succeed. MPEP § 2145 X.B. prohibits rejections under this theory. Indeed, it is only through the teachings of the present specification that one of ordinary skill in the art would gain a reasonable expectation of success in treating solid tumors with a synergistic combination of camptothecin, or a camptothecin derivative, and a topoisomerase II inhibitor. However, as mentioned above, Applicant's own disclosure cannot provide the motivation or expectation of success necessary to render a claim obvious.

Therefore, because Furuta *et al.* does not provide an adequate motivation or reasonable expectation of achieving the presently claimed invention, Applicant respectfully submits that the presently claimed invention would not be obvious over Furuta *et al.* Accordingly, Applicant respectfully requests that the Office reconsider and withdraw the rejection of claims 5-8 and 13-20 under 35 U.S.C. § 103(a).

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C. Conclusion

In view of the fact that Furuta *et al.* fails to disclose or suggest all of the elements of the present claims, and the fact that Furuta *et al.* fails to provide a motivation or a reasonable expectation of success in making a synergistically effective composition comprising a synergistically effective composition of camptothecin, or a camptothecin derivative, and a topoisomerase inhibitor, or in treating solid tumors with such a composition, Applicant respectfully submits that the presently claimed invention is not anticipated by, and is not rendered obvious by, Furuta *et al.* Therefore, Applicant respectfully requests that the Office reconsider and withdraw the rejection of claims 1-7 and 9-12 under 35 U.S.C. § 102(b), and claims 5-8 and 13-20 under 35 U.S.C. § 103(a).

II. *Conclusion*

For at least the reasons given above, Applicant respectfully submits that the present claims are neither anticipated nor rendered obvious by Furuta *et al.* Accordingly, Applicant respectfully submits that claims 1-20 are in condition for allowance.

If the Examiner believes anything further is necessary in order to place the claims in even better condition for allowance, Applicant respectfully requests that the Examiner contact her undersigned representative at the telephone number or e-mail address listed below.

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Please grant any extensions of time required to enter this response and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, L.L.P.

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Attachment:
Appendix

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APPENDIX
(accompanying Amendment of November 13, 2002)

09/809,329

IN THE CLAIMS:

Please amend claims 1, 2, 11, and 13 as follows:

1. (Amended) A synergistic therapeutic pharmaceutical composition[,] for solid tumors comprising an effective amount of camptothecin, or a camptothecin derivative, in combination with an effective amount of a topoisomerase II inhibitor, wherein said composition provides a synergistic effect in [for] the treatment of solid tumors.

2. (Amended) A synergistic therapeutic pharmaceutical composition[,] for solid tumors comprising an effective amount of CPT-11[,] in combination with an effective amount of a topoisomerase II inhibitor, wherein said composition provides a synergistic effect in [for] the treatment of solid tumors.

11. (Amended) A synergistic therapeutic pharmaceutical composition[,] for solid tumors comprising an effective amount of at least two agents, wherein [at least one] a first agent is CPT-11[, in combination with an effective amount of at least one second agent, wherein said second] and a second agent is doxorubicin, [for] wherein said composition provides a synergistic effect in the treatment of solid tumors.

13. (Amended) A method of treating a solid tumor, comprising administering an effective amount of camptothecin, or a camptothecin derivative, as a first agent, in

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combination with [administration of] an effective amount of a topoisomerase II inhibitor as a second agent, wherein the agents are administered simultaneously, semi-simultaneously, or separately, and wherein said first and second agents provide a synergistic effect in the treatment of said solid tumor.

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